WHAT IS CLAIMED IS:

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- 1. Use of a humanized antibody to alpha-4 integrin in
- the manufacture of a medicament for treating a disease
- 3 selected from the group consisting of asthma, atherosclerosis,
- 4 AIDS dementia, diabetes inflammatory bowel disease,
- 5 rheumatoid arthritis, transplant rejection, graft versus host
- 6 disease, tumor metastasis nephritis, atopic dermatitis,
- 7 psoriasis, myocardial ischemia, and acute leukocyte mediated
- 8 lung injury.
- 1 2. The use according to claim 1, wherein the disease is 2 asthma.
- 3. The use according to claim 1, wherein the disease is atherosclerosis.
- 1 4. The use according to claim 1, wherein the disease is 2 AIDS dementia.
- 5. The use according to claim 1, wherein the disease is diabetes.
- 1 6. The use according to claim 1, wherein the disease is 2 inflammatory bowel disease.
- 7. The use according to claim 1, wherein the disease is rheumatoid arthritis.
- 8. The use according to claim 1 wherein the disease is
 2 transplant rejection.
- 9. The use according to claim 1, wherein the disease is graft versus host disease.
- 1 10. The use according to claim 1, wherein the disease is 2 tumor metastasis.

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- 1 11. The use according to claim 1, wherein the disease is 2 nephritis.
- 1 12. The use according to claim 1, wherein the disease is 2 atopic dermatitis.
- 1 13. The use according to claim 1, wherein the disease is 2 psoriasis.
- 1 14. The use according to claim 1, wherein the disease is 2 myocardial ischemia.
 - 15. The use according to claim 1, wherein the disease is acute leukocyte-mediated lung injury.
- 1 16. The use according to claim 17, wherein the disease 2 is adult respiratory distress syndrome.
 - 17. The use according to any one of the preceding claims wherein the humanized antibody is a humanized form of the mouse 21.6 antibody.
- 1 18. The use according to claim 17, wherein the humanized 2 antibody comprises a humanized heavy chain and a humanized 3 light chain:
- (1) the humanized light chain comprising three
 complementarity determining regions (CDR1, CDR2 and CDR3)
 having amino acid sequences from the corresponding
 complementarity determining regions of the mouse 21-6
- 8 immunoglobulin light chain variable domain designated SEQ. ID.
- 9 No. 2, and a variable region framework from a human kappa
- 10 light chain variable region framework sequence except in at
- 11 least one position selected from a first group consisting of
- 12 L45, L49, L58 and L69, wherein the amino acid position is
- 13 occupied by the same amino acid present in the equivalent
- 14 position of the mouse 21-6 immunoglobulin light chain variable
- 15 region framework; and

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the humanized heavy chain comprising three 16 complementarity determining regions (CDR1, CDR2 and CDR3) 17 having amino acid \sequences from the corresponding 18 complementarity determining regions of the mouse 21-6 19 immunoglobulin heavy chain variable domain designated SEQ. ID. 20 No. 4, and a variable region framework from a human heavy 21 chain variable region framework sequence except in at least 22 one position selected\from a second group consisting of H27, 23 H28, H29, H30, H44, H71, wherein the amino acid position is 24 occupied by the same amino acid present in the equivalent 25 position of the mouse 2176 immunoglobulin heavy chain variable 26 region framework; 27

wherein the humanized immunoglobulin specifically binds to alpha-4 integrin with a binding affinity having a lower limit of about $10^7~{\rm M}^{-1}$ and an upper limit of about five-times the binding affinity of the mouse 21-6 immunoglobulin.

- 19. The use according to claim 18, wherein the humanized light chain variable region framework is from an RE1 variable region framework sequence except in at least one position selected from the first group, and except in at least one position selected from a third group consisting of positions L104, L105 and L107, wherein the amino acid position is occupied by the same amino acid present in the equivalent position of a kappa light chain from a human immunoglobulin other than RE1.
- 20. The use according to claim 19 wherein the humanized heavy chain variable region framework is from a 21/28 CL variable region framework sequence.
- 21. The use according to claim 20, wherein the humanized light chain variable region framework comprises at least three amino acids from the mouse 21.6 immunoglobulin at positions in the first group and three amino acids from the kappa light chain from the human immunoglobulin other than REI at positions in the third group, and the humanized heavy chain variable region framework comprises at least five amino acids

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from the mouse 21.6 immunoglobulin at positions in the second 8 group. 9

- The use according to claim 21, wherein the humanized 1 light chain variable region framework is identical to the RE1 2 light chain variable region framework sequence except for the 3 at least three positions from the first group and the three 4 positions from the third group, and the heavy chain variable 5 region framework is identical to the 21/28'CL heavy chain 7 variable region framework sequence except for the at least five positions from the second group.
 - 23. The use according to claim 22, wherein the at least three positions from the first group are positions L45, L58 and L69, and at the least five positions from the second group are positions H27, H28, H29, \H30 and H71,
- The use according to claim 23, wherein the humanized light chain comprises complementarity determining regions that 2 are identical to the corresponding complementarity determining regions of the mouse 21-6 heavy chain, and the humanized heavy chain comprises complementarity determining regions that are 5 identical to the corresponding complementarity determining regions of the mouse 21-6 heavy chain, except that the CDR3 7 region of the humanized heavy chain may or may not comprise a 8 phenylalanine residue at position H9&. 9
- The use according to claim 24, wherein the amino 1 acid sequence of the mature light chain variable region is the 2 sequence designated La (SEQ. ID NO:7) in Fig. 6 and the amino 3 acid sequence of the mature heavy chain variable region is Ha 4 (SEQ. ID NO:11) in Fig 7. 5
- The use according to claim 25, wherein the humanized 1 antibody is a Fab fragment. 2

